

## RATIONAL TESTING

### Investigating hypertension in a young person

Fabian Hammer, Paul M Stewart

Where do you start when checking for secondary causes of hypertension in a young adult? This article will guide you through key tests and imaging techniques

Institute of Biomedical Research,  
Division of Medical Sciences,  
University of Birmingham,  
Birmingham B15 2TT

Correspondence to: P M Stewart,  
[p.m.stewart@bham.ac.uk](mailto:p.m.stewart@bham.ac.uk)

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#### The patient

A 27 year old man with a six month history of mild but progressive headache visited his general practitioner and was found to have a blood pressure of 178/108 mm Hg. He had an unremarkable medical history, but his father had had high blood pressure and had died from a stroke at age 45 years. Clinical examination with a particular emphasis on the cardiovascular system including funduscopy was unremarkable, and no renal artery bruit was heard. Basic laboratory tests at his general practice were all normal (sodium 144 (normal range 135-145) mmol/l; potassium 3.8 (3.5-5.1) mmol/l; creatinine 105 (60-110)  $\mu$ mol/l; urea 5.4 (2.9-9.4) mmol/l), with no proteinuria.

#### What is the next investigation?

Arterial hypertension warrants further investigations to exclude secondary causes of hypertension in young people (aged <40 years), those with blood pressure resistant to antihypertensive treatment, and those with a family history of hypertension or stroke at age <50 years. Furthermore, a detailed social history, including alcohol intake and substance misuse (such as cocaine) might show reversible contributors of increased blood pressure.

Before further investigations the diagnosis of arterial hypertension needs to be established by blood pressure measurements on at least three occasions using a sphygmomanometer with an appropriate cuff size for arm circumference (cuffs that are too small will give false high readings). If white coat hypertension is suspected a 24 hour ambulatory blood pressure measurement is warranted.

#### Urea, creatinine, electrolytes, and urine analysis

All patients with diagnosed arterial hypertension must have urea and electrolytes and urine analysis performed to screen for hypokalaemia and renal disease as these basic laboratory tests are widely available and cost effective and if abnormal will give important hints on which

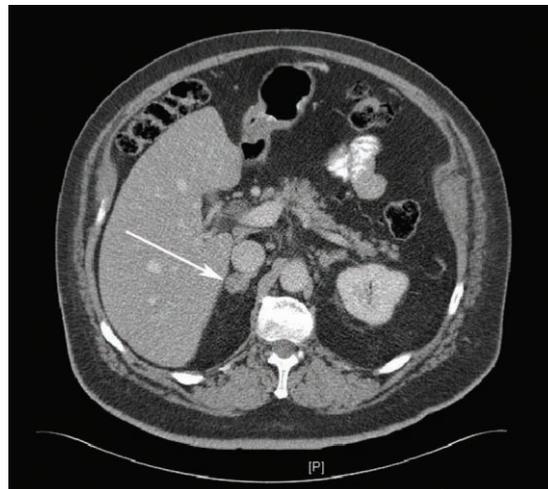
test to perform next. Although only a third of patients with subsequently confirmed primary hyperaldosteronism exhibit frank hypokalaemia, potassium concentrations in the remaining two thirds of patients with hyperaldosteronism are usually at the lower end of the reference range and sodium concentrations at the higher end.

#### Renal ultrasonography, electrocardiography, chest radiography

In our patient, normal kidney function, electrolytes, and the absence of proteinuria strongly argues against renoparenchymal disease, and so renal ultrasonography is of limited benefit. Electrocardiography and chest radiography in this patient may be entirely normal, but if hypertension is longstanding they may show signs of left ventricular hypertrophy. These investigations are of limited value in establishing the underlying cause.

#### Measurement of plasma aldosterone and renin

Primary hyperaldosteronism is now considered to be the most prevalent form of secondary hypertension, accounting for 5-10% of all hypertensive patients.<sup>1,2</sup> Screening for primary hyperaldosteronism is based on a high plasma aldosterone concentration and suppressed plasma renin activity, giving a high ratio of plasma aldosterone concentration to plasma renin



Computed tomogram of the abdomen showing a right adrenal Conn's adenoma measuring 16 mm x 19 mm (arrow)

This article is the first in a series of occasional articles providing an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School.

## LEARNING POINTS

Primary hyperaldosteronism accounts for up to 10% of all hypertensive patients and is considered to be the most prevalent form of secondary hypertension

Screening for primary hyperaldosteronism is based on the ratio of plasma aldosterone to renin

Potassium concentration is often normal in primary hyperaldosteronism, and so hypokalaemia must not be a prerequisite for screening

Antihypertensive drugs do not have to be stopped routinely before screening

activity. Although the exact cut-off values depend on the laboratory and assays used, a ratio of  $>750$  (aldosterone in pmol/l and plasma renin activity in ng/ml/h) with an absolute aldosterone concentration of  $>400$  pmol/l is highly suggestive of primary hyperaldosteronism.<sup>3</sup>

Antihypertensive drugs do not have to be stopped routinely before these measurements are conducted (except for spironolactone, eplerenone, and amiloride) but in some patients may contribute to false positive and negative results. A positive screening test warrants a hospital referral, firstly to confirm the diagnosis (usually with oral or intravenous sodium loading or a fludrocortisone suppression test) and secondly to differentiate between the two principal causes—namely, a unilateral aldosterone producing adenoma (or Conn's adenoma) and idiopathic hyperaldosteronism, for which selective adrenal venous sampling remains the optimal test. Catheterisation of the adrenal veins (particularly the right vein) even in the most experienced hands remains technically challenging and should therefore be performed only in specialist centres.

#### 24 hour urinary-free catecholamines or plasma-free metanephrines

Tumours that produce catecholamine, such as pheochromocytomas and paragangliomas, are rare (found in 0.1-0.6% of hypertensive patients). However, they form an important differential diagnosis in our patient even if only mild headaches and no other classic symptoms (paroxysms of palpitations, sweating, and pallor) are present. Testing for plasma-free metanephrines is now considered to be the optimal test (sensitivity 99%, specificity 86%), but given its limited availability screening is still predominantly based on excretion of urinary catecholamines (adrenaline, noradrenaline, dopamine,

metanephrine, normetanephrine, and vanillylmandelic acid) (sensitivity 86%, specificity 88%).<sup>4</sup> False positive test results can be prevented if the patient avoids consumption of caffeine, nuts, and chocolate for 24 hours before and during urine collection.

#### Renal imaging

Magnetic resonance angiography has now become the investigation of choice (sensitivity and specificity  $>90\%$ ) to rule out renovascular abnormalities (namely, renal artery stenosis),<sup>5</sup> in which case hypertension develops as a result of renal hypoperfusion. In the absence of a renal artery bruit, magnetic resonance angiography should be performed only if laboratory screening tests for primary hyperaldosteronism and phaeochromocytoma are negative.

#### Outcome

In this patient, blood tests showed a raised plasma aldosterone concentration of 712 (normal range 28-445) pmol/l and a suppressed plasma renin activity of 0.2 (0.7-5) ng/ml/h with a ratio of 3560 (normal ratio  $<750$ ), therefore highly suggestive of primary hyperaldosteronism. Aldosterone concentrations remained raised at 462 pmol/l after a saline infusion study that confirmed the diagnosis of primary hyperaldosteronism. Subsequent computed tomography showed a solitary, well defined lesion of 2 cm in the right adrenal gland, which was removed by laparoscopic adrenalectomy (figure). Blood pressure returned to normal.

We thank Peter Guest for the figure.

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## Trial registration: advice to authors

In accordance with the International Committee of Medical Journals Editors (ICMJE) uniform requirements for manuscripts submitted to biomedical journals, the *BMJ* will not consider reports of clinical trials unless they were registered prospectively before recruitment of any participants. This applies to trials that started after 1 July 2005: for older trials, retrospective registration will be acceptable, but only if completed before submission of the manuscript to the journal.

Eligible trials have been defined by ICMJE since 1 July 2008 as “where human participants are prospectively assigned to one or more health-related interventions [including health services and behavioural interventions] to evaluate the effects on health outcomes”; before that,

they were defined more narrowly as trials “where human participants are prospectively assigned to investigate the cause and effect relationship between a medical intervention and health outcome.”

The *BMJ*'s criteria for a suitable public trial registry are: free to access, searchable, and identifies trials with a unique number; registration is free or has minimal cost; registered information is validated; registered entry includes details to identify the trial and investigator and includes the status of the trial; and the research question, methodology, intervention, funding, and sponsorship must all be disclosed at registration.

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## THE COMPETENT NOVICE

# Practising safely in the foundation years

Susannah Long, Graham Neale, Charles Vincent

Clinical Safety Research Unit,  
Imperial College, St Mary's  
Hospital, London W2 1NY

Correspondence to: S Long  
s.long@imperial.ac.uk

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Junior doctors are vital to promoting quality of care and safety for patients. This article outlines strategies to reduce errors and subsequent harm

Many junior doctors may not be aware that about one in 10 acute hospital admissions in the United Kingdom is associated with at least one adverse event, occasions on which patients are harmed by their medical management rather than the illness itself.<sup>1,2</sup> About half of these adverse events are thought to be preventable, and a third are associated with serious disability or

death. More commonly, less serious incidents cause inconvenience and discomfort for the patient and can lead to a longer stay in hospital—see the first scenario box about Mrs Jones (case scenario: part 1). Junior doctors are at the front line of patient care and therefore play a crucial role in reducing harm to patients. This is why patient safety is an integral part of the Foundation Curriculum ([www.foundationprogramme.nhs.uk](http://www.foundationprogramme.nhs.uk)).

### Why do things go wrong?

Studies of errors in health care and other industries have led to a much broader understanding of their cause, with less focus on the individual who makes the error and more on the wider system and organisational factors.<sup>3</sup> An action or omission may be easily identified as the immediate cause of an incident, but closer analysis usually reveals a series of events leading up to it, as in the case of Mrs Jones. We might simply blame the junior doctor for not checking the international normalised ratio (INR) before prescribing, but a little reflection provides a more complex picture. Mrs Jones's admission to hospital with delirium and falls was the result of recognised complications of treatment with tramadol and bendroflumethiazide; in her confused state she took too much warfarin at home. However, her clinical problems were compounded by various problems with her health care. The table shows some of the causes and contributory factors that led to the adverse event in this case, and some general reflections.

Several lessons arise from the management of this frail elderly patient. Mrs Jones was seen by a junior doctor with no experience of prescribing warfarin, a problem that ultimately stems from training and staffing decisions. This doctor may have been either unwilling or unable to seek senior help or perhaps was not aware of the dangers of the situation. Perhaps she was not supported adequately by her seniors, who ought to have encouraged her to ask about anything she was even

### CASE SCENARIO: PART 1

Mrs Jones was a 90 year old woman living alone. Before admission she had been taking warfarin for atrial fibrillation and bendroflumethiazide 2.5 mg once daily for hypertension. She had been increasingly troubled by pain from osteoarthritis of her knees. She had been finding it difficult to climb the stairs at home and to shop, even with the use of her stick, and was requiring more help from her niece. Recently her general practitioner added tramadol 50 mg four times a day to her existing analgesia (paracetamol 1 g four times a day).

A week later she was admitted to hospital after being found on the floor by her niece. She was acutely confused, and her niece said that although Mrs Jones's memory had been failing recently, she had been much more muddled over the past few days.

The admitting doctor recognised that Mrs Jones had delirium, probably caused by a combination of tramadol, hyponatraemia, and constipation associated with opioids, and treated her accordingly. However, the doctor was not aware that Mrs Jones was taking warfarin, and the international normalised ratio was not measured.

Later in the evening, the first year foundation (F1) doctor on call for medicine was asked to prescribe warfarin by the nursing staff, as Mrs Jones's niece informed them that she had been taking this. In the absence of an international normalised ratio, and with no knowledge of Mrs Jones's usual dose, the F1 doctor prescribed 5 mg for the next three evenings, thinking this was a typical dose.

Three nights later, Mrs Jones tried to go to the toilet and fell, sustaining a large haematoma to her leg. Her international normalised ratio was checked, and to the dismay of the F1 doctor it was >10. Later it emerged that Mrs Jones had also been taking too much warfarin at home while she was unwell. After correction of her international normalised ratio, Mrs Jones required surgical evacuation of her haematoma and a prolonged period of rehabilitation before being discharged home.

### CASE SCENARIO: PART 2

The F1 doctor's consultant was fully supportive, helping her to complete a critical incident form and talking through the adverse event with her and the team. The F1 doctor consequently learnt how to deal with anticoagulation safely and about the risks associated with delirium. The consultant and the F1 doctor apologised and gave a full explanation to Mrs Jones and her niece. After a discussion of the risks and benefits, Mrs Jones decided not to start taking warfarin again.

This series aims to help junior doctors in their daily tasks and is based on selected topics from the UK core curriculum for foundation years 1 and 2, the first two years after graduation from medical school

**Box 1 Examples of strategies that have been developed to reduce errors and subsequent harm**

**Simplification and standardisation of clinical processes**

A longitudinal study found significantly fewer errors of radiographic interpretation in an emergency department after simplifying and redesigning the system of communication between staff<sup>5</sup>

**Checklists and aide memoires**

A collaborative cohort study in intensive care units in Michigan showed that a multicomponent intervention, which included the use of a checklist to ensure adherence to infection control practices, substantially reduced central line infections<sup>6</sup>

**Information technology**

In preventing adverse drug events, electronic prescribing markedly reduces medication errors, and computerised alerts ensure that orders to monitor drug levels are implemented after drugs are prescribed.<sup>7</sup> In addition, bar coding substantially reduces transfusion errors<sup>8</sup>

**Team training to reduce errors**

A prospective multicentre study in emergency departments showed that the use of team training similar to that used in aviation resulted in improved communication and fewer errors<sup>9</sup>

**Risk management programmes**

Clinical risk management programmes, in which adverse events are detected in a hospital and action is taken to reduce their occurrence, produce a steady reduction in harm to patients if sustained over many years<sup>10</sup>

**Mechanisms to improve uptake of evidence based treatment patterns**

Care bundles (groups of evidence based interventions that have a more positive effect when implemented together than when implemented individually) are one way of achieving uptake of evidence based treatment patterns. For example, “sepsis bundles” have been used to implement the international guidelines for improving the management of severe sepsis produced by the Surviving Sepsis campaign.<sup>11,12</sup>

slightly unsure about. The risks to Mrs Jones were probably further heightened by poor communication within the hospital team and with primary care, inadequate staffing levels, and even the design of the ward, which meant that she could not be easily observed by nursing staff. Recognising this confluence of factors has led to patient safety being regarded as a systems matter rather than a case of “who made the mistake?”

**How can we make health care safer?**

We need to think about the entire healthcare system to make health care safer. This requires action on many levels, from patient involvement and the training of individual staff right up to the organisation of health care and the design of hospitals. Box 1 outlines examples of various strategies that have been developed to reduce errors and subsequent harm<sup>1</sup>; these examples show what can be achieved by changing the way health care is delivered. However, safety also relies on the attitudes, skills, and courage of clinical staff, and this is where junior doctors make a critical contribution.

**What are the challenges for junior doctors to practising safely?**

Trainees are busy, inexperienced, and often fatigued, and they may feel inadequately equipped or supervised. They are likely to become involved in adverse events while still trying to come to terms with the hospital system. Moreover, although all newly qualified doctors should be aware of the importance of teamwork, they may find communication difficult in medical and nursing hierarchies. Trainee doctors nevertheless need to understand the risks of practising hospital medicine and how to minimise the impact of these risks.

**How can junior doctors improve patient safety?**

Although junior doctors may think that they can do little to prevent errors caused by “system” problems, they are part of the buffer between patients and the system—the final line of defence against harm. Newly qualified doctors therefore need to have a strong sense of risk awareness from their very first day. Box 2 outlines suggestions for how junior doctors could try to improve the safety of their patients; some are matters of common sense, but others are markers of expertise and a mature approach to practice. Box 3 gives further advice on drugs and prescribing.

**Background to the scenario “some of the causes and contributory factors that led to the adverse event in Mrs Jones’s case”**

Problem	Why did this happen?	Reflection
Delirium and fall at home	A combination of tramadol, hyponatraemia, and constipation	<i>Risk assessment and anticipation of side effects</i> Common drugs such as tramadol and bendroflumethiazide have predictable side effects, such as constipation and hyponatraemia respectively. The side effects of these drugs can be particularly potent in elderly people and should always be considered and treated pre-emptively where possible
The international normalised ratio was not measured on admission	The admitting team was not aware that Mrs Jones was taking warfarin	<i>Clinical history</i> Make every effort to collect all necessary information, particularly the drug history, on admission; this may require contacting the general practitioner, nursing home, and family. Check for electronic discharge summaries from previous admissions. Emergency patients often arrive at the hospital without medication lists, so encourage families to keep and update medication lists
Warfarin was prescribed without checking the international normalised ratio	The F1 doctor was worried about the risk of stroke if Mrs Jones did not receive her anticoagulation that evening	<i>Inexperience</i> The F1 doctor had never prescribed warfarin before <i>Guidelines</i> Most NHS trusts provide protocols and guidelines for common clinical procedures, such as anticoagulation at induction, often in the form of a handbook for junior doctors and usually on the trust’s intranet. The F1 doctor could have consulted these <i>Supervision</i> The F1 doctor felt that this was too trivial a matter to check with her seniors. Perhaps her seniors could be more supportive and encouraged her to ask about even seemingly trivial matters, particularly as this was her first day on call <i>Working conditions</i> This was the F1 doctor’s first day on call and she felt under a lot of pressure from being frequently bleeped <i>Team factors</i> The nurses on the ward were finding it difficult to look after Mrs Jones because she was disoriented. The nurses and Mrs Jones’s niece were pressurising the F1 doctor to prescribe warfarin, making it harder for her to say that she would prefer to wait until an international normalised ratio had been checked. The ward pharmacist and nurses did not notice that the warfarin had been prescribed in the absence of an international normalised ratio
Fall on the ward, causing injury	Mrs Jones had delirium and was in an unfamiliar environment	<i>Hospital environment</i> Patients with delirium should be nursed in a well lit, quiet environment and be in a position where they can be observed by the nurses. <sup>4</sup> This was not possible on this ward <i>Staffing levels</i> Staff absence and sickness had reduced the level of monitoring of patients

**Box 2 Tips for practising safely****Internal alarm bells**

When caring for patients, try to develop your internal alarm bells. If you feel that something is “not right” or you are uncomfortable or worried about a clinical situation, acknowledge your feelings and ask for help.

**Feeling overwhelmed**

If you feel overwhelmed, note that it is not necessarily a sign of weakness, but rather a natural reaction to a high pressure situation. Don't hesitate to ask for help if this occurs—in the long run you will be happier that you ensured safety for your patients than saved yourself embarrassment.

**Clinical guidelines**

Use clinical guidelines where available. A systematic review of the effect of clinical guidelines on practice has shown that use of evidence based guidelines reduces harm to patients,<sup>13</sup> although they must be used while assessing their appropriateness in each patient's context.<sup>14</sup> Specific prescribing guidelines are particularly helpful for junior doctors; at induction most NHS trusts will provide such guidance about common topics such as anticoagulation. Often such information is provided on trusts' intranet sites for easy access.

**Documentation**

Always document your thought processes, actions, and plans, including the responsibilities of members of medical and nursing teams and the mode of follow-up, and ensure adequate handover.<sup>15-16</sup> For example, in the case scenario of Mrs Jones the first year foundation (F1) doctor who was asked to prescribe warfarin may have written in the notes: “Asked to prescribe warfarin, but no baseline INR available. Plan—INR sample sent, withhold warfarin until result available—I will check result later.” Such a plan should be explained to the nursing staff and the patient.

**Checking results and all recorded information**

Check results of outstanding investigations daily. If you are not sure how to interpret the result or what to do with an abnormal result, ask your seniors. When assessing a patient, try to find and read through all the information that the nurses have recorded, including fluid balance charts, stool charts, and basic observations.

**Speaking up if an error is suspected**

Don't be afraid to speak up if you think something may go wrong or has gone wrong—trainee doctors are in a key position to see and report untoward incidents. It is vital that you raise any areas of concern with your seniors and report any clinical incidents. All trusts have confidential reporting systems. Individual departments of risk management will record reported incidents and investigate as necessary and will submit them anonymously to the National Reporting and Learning System of the National Patient Safety Agency ([www.npsa.nhs.uk/patientsafety/reporting/](http://www.npsa.nhs.uk/patientsafety/reporting/)); in addition, any employee of the NHS can use this reporting system online. The information reported in this way is used to identify patterns and trends in patient safety issues and to help develop solutions, which are then fed back to the NHS trusts. There is evidence that trusts in which there are high levels of such reporting tend to have a stronger safety culture and receive fewer complaints than others.<sup>17</sup>

**Box 3 Safe prescribing**

- When taking a history obtain a complete list of medications, even if this means telephoning the general practitioner, care home, or relative. Also, try to gauge if the patient has been taking their medications as prescribed and whether anything has changed recently that may explain their symptoms
- As drug related adverse events are common (affecting 2-14% of all patients admitted to hospital<sup>18</sup>), consider the necessity for and the potential side effects of each drug as you write up the drug chart
- Don't feel unduly pressurised by others to give a treatment when you are not sure it is the correct treatment for that patient or you do not feel experienced enough to give it
- Be particularly wary with vulnerable, complex patients such as Mrs Jones. Always consider whether it is really necessary to prescribe any drug, and if you believe it is, give the lowest possible dose—“start low, go slow”

**What to do after an adverse event**

Three things are essential to think about when an adverse event has occurred. Firstly, protect the patient from further harm, reverse any damage you can, and call for senior help. Secondly, look after the patient, family, and staff who may have been involved. Your seniors should support you, talk through the incident with you and other staff, and help with the vital task of apologising and providing an explanation to the patient. A prompt apology and full explanation of events and the likely short and long term effects should always be given.<sup>15</sup> Doctors should not be afraid to apologise—according to the NHS Litigation Authority, an apology is not an admission of liability.<sup>19</sup> A timely apology and explanation help the patient come to terms with what has happened (and also reduces the chance they will complain).<sup>20</sup> Thirdly, record and report the incident and consider what can be learnt from it, as described above. Further advice on what to do after an adverse event, how to achieve effective apologies, and prevention of complaints is in another article in this series.<sup>21</sup>

**Conclusion**

Junior doctors are vital to promoting quality of care and safety. Ongoing research into this complex area

**LEARNING POINTS**

Adverse events are common, particularly in vulnerable patients such as older people

Junior doctors are at the front line of patient care and therefore play a crucial role in reducing harm to patients

If a junior doctor is at all worried about a patient, it is their responsibility to seek help

Junior doctors should discuss and report adverse events, with the aim of learning from them

It is vital that a full apology and explanation be given to the patient when an adverse event occurs

aims to provide clearer solutions, but in the meantime we should all be vigilant about the risks of medical practice and adhere to basic principles to minimise these. We need to acknowledge too that no matter how hard we aim for high quality care, adverse events will inevitably happen, and we need to use them for learning rather than for blame.

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## CORRECTIONS AND CLARIFICATIONS

### NHS at 60—Universality, equity, and quality of care

An error occurred in the second article of this series on the NHS by Tony Delamothe (*BMJ* 2008;336, print publication 7 Jun, 1278-81). The article wrongly states that Oxfordshire Primary Care Trust spent the least on cancer per cancer patient in 2006-7 (in fact, Dorset did). This error arose from a mistake in the Department of Health's cancer-spend data for 2006-7 (an error now acknowledged by the department) that was reiterated in a recent *Civitas Review* article, from which Delamothe drew this information.

### Prolapsed intervertebral disc

In the second paragraph of this editorial by Jeremy Fairbank (*BMJ* 2008;336, print publication 14 Jun, 1317-8), the second sentence should have read: "Surgery should be performed before eight weeks only in patients with progressive neurological deficit who have a disc prolapse that can be detected by magnetic resonance imaging consistent with the neurology" [and should not have ended "...only in patients with progressive neurological deficit, which can be detected by magnetic resonance imaging"].

### Obituary: Wallace William Brigden

In this obituary of Wallace William Brigden by Caroline Richmond, the final sentence—about his family—was inaccurate (*BMJ* 2008;336, print publication 14 Jun, p 1382). He is indeed survived by his wife, Everel, a retired general practitioner, but he also leaves not "three sons" but two sons and a daughter from his first marriage and a son and stepson from his second.

### Harms of target driven health care

In this Personal View by Nigel Rawlinson (*BMJ* 2008;337: a885, print publication 26 Jul, p 237), the last sentence of the third paragraph became scrambled during editing. It should read: "Without this time pressure they [the patients] might have stayed longer, their condition might have been better stabilised, and they might have been transferred to a more appropriate clinical area."

### Obstetricians seek recognition for Chinese pioneers of safe abortion

In this News article by Rebecca Coombes (*BMJ* 2008;336, print publication 14 Jun, p 1332-3) we did not make clear that neither Roger Short nor Joyce Leong are obstetricians, as readers might have assumed from the title and the text. Short is professorial fellow in the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne, Australia. Leong was a final year medical student at the University of Melbourne when she went to Thailand to study vacuum aspiration abortion and when she wrote the paper; she has since qualified as a doctor and is doing her internship in Australia.

### Obituary: Fyodor Grigorievich Uglov

The author of the obituary of Fyodor Grigorievich Uglov (*BMJ* 2008;337:a866, print publication 2 Aug, p 300) was inadvertently omitted from the print issue and the pdf of the print issue during the process of cutting text to fit the page. The author is Boleslav Lichterman.